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CYCLIC NUCLEOTIDES IN TISSUES DURING LONG-TERM HYPOKINESIA

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Translation of "Tsiklicheskiye nukleotidy v tkanyakh pri dlitel'noy gipokinezii," Voprosy meditsinskoy khimii, Vol. 27, No. 1, 1981, pp. 59-61.

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16. Abstract

Male Wistar rats were kept hypokinetic by placing them in small containers for 22 days. Blood plasma cAMP content was subsequently found increased, and cGMP content decreased, in the experimental animals. Liver and thymus cAMP content was similar in the control and experimental animals. There was a 20 and 38% decrease of cAMP content in the kidneys and spleen, respectively. Hypokinesia's reduction of cyclic nucleotides seems to inhibit RNA and protein synthesis.

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CYCLIC NUCLEOTIDES IN TISSUES DURING LONG-TERM HYPOKINESIA

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A prolonged hypokinetic state leads to serious disorders in the /59* body [1]. It has been shown that hypokinesia is accompanied by dystrophic changes in muscles and disruption of protein, water-salt, and other /60 types of metabolism. In addition, changes are seen in the activities of numerous enzymes, and catecholamine and corticosterone metabolisms are severely disrupted.[2]. According to current ideas, the actions of many hormones in the cell are implemented through a system of cyclic nucleotides. These compounds play an important role in such primary cell vital processes as proliferation, transcription, and translation.

Information on tissue cyclic nucleotide content during hypokinesia is quite exiguous [3]. In this connection, our goal was to study cAMP and cGMP levels in certain tissues of rats kept under conditions limiting their mobility.

Methodology

The experiments were done using male Wistar rats weighing 200-250 g. The experimental animals were kept for 22 days in special containers sharply restricting their mobility [4]. The control animals were kept in the same type of confinement and were furnished the same diet as the experimental animals. The general condition of the animals was checked periodically during the course of the experiment. Food consumption was virtually identical for the control and experimental animals. The rats were decapitated, blood was collected from each and placed in a test tube with 0.5 M EDTA, and after centrifugation we obtained the plasma in which cAMP and cGMP content was ascertained.

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*Numbers in the margin indicate pagination in the foreign text.

To determine cyclic nucleotides in the liver, kidneys, spleen, and thymus, the tissues were frozen with liquid nitrogen and cAMP was extracted using the method of Tsang et al. [5]. Cyclic nucleotide content was determined with the radioimmunologic method, using standard reagent samples from the "Amersham" Company (England). Test radioactivities were counted in an SL-30 liquid scintillation counter (France). The amount of cAMP in the tissues was expressed in picomoles per mg moist tissue, and plasma amounts were given in picomoles per ml.

Results and Discussion

The results of the experiment indicated that the weights of the experimental animals lagged 17% behind the controls following the 22-day hypokinesia, which concurs with literature data [6]. Absolute weights of the thymus, spleen, liver, and kidneys in the experimental animals also were lower than in the controls, by 34, 39, 32, and 14%, respectively.

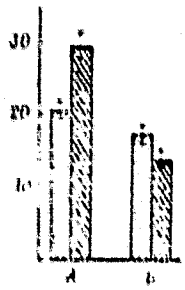
Data on blood plasma cyclic nucleotide contents are given in the figure, from which we can see that restricting the motor activity of the animals led to altered cAMP and cGMP levels in blood plasma. cAMP content had a statistically significant rise of 47% in the experimental animals, relative to the controls, while cGMP levels decreased 18%, i.e., the changes in the nucleotides during hypokinesia were of an opposite nature. We should note that the ratio of cAMP to cGMP often is reciprocal and evinced thusly in a number of tissues [7, 8].

cAMP CONTENT (in pmol/mg) IN RAT TISSUES FOLLOWING HYPOKINESIA

Tissue	Control	Hypokinesia
Liver (9)	0,46±0,02	0,43±0,03
Thymus (9)	1,24±0,01	1,26±0,06
Kidneys (8)	0,71±0,003	0,56±0,01
p		<0,01
Spleen (9)	1,47±0,48	2,89±0,51
p		<0,1

Note: Number of tests in parentheses.

The ratio of cAMP to cGMP was /61 higher (2/10) in the experimental animals than in the controls (1/18). This may be evidence of the increasing role of adrenergic factors under the influence of hypokinesia, since it is known that cAMP is specifically sensitive to the action of neuromediators (norepinephrine), while cGMP is sensitive to cholinergics (acetylcholine).



Cyclic nucleotide content (in pmol/ml) in the blood plasma of rats affected by hypokinesia.

A -- cAMP; B -- cGMP. Lighter columns -- controls, hatched columns -- hypokinesia.

It follows from the data in the table that restriction of mobility affected cAMP content in the tissues under study in different ways. In the livers of the experimental animals, for instance, cAMP content was not significantly different than in the controls'. Similarly, no differences were noted between cAMP contents in the thymuses of control and experimental animals. In the kidneys and spleen, however, cAMP levels were below normal after hypokinesia. cAMP levels in the kidneys of the experimental animals were significantly diminished by 20%, and cAMP levels in the spleen were decreased somewhat more (by 38%). Thus cyclic nucleotide metabolism has different features in each organ under the influence of hypokinesia.

The data we obtained on cAMP reduction in the kidneys and spleen during movement restriction agree with the concept of hypokinesia as a factor suppressing most biologic processes.

Since cAMP is an important mediator between membrane and intracellular enzymes, change in its concentration during hypokinesia may lead to disruptions in numerous processes it governs. Cyclic nucleotides are known to play a vital role in protein synthesis and nucleic acid control mechanisms. According to literature data, protein and RNA synthesis is suppressed in many animal tissues when mobility is restricted [9, 10]. The data obtained in this experiment allow us to presume that reduction of cAMP levels may be of decisive importance in the disruption of these processes.

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